REMARKS

Reconsideration of the instant application in view of the above amendments and the following remarks is respectfully requested. As of the mailing date of the Office Action dated July 25, 2007, claims 5-26 were pending and non-elected claims 17-26 were withdrawn from consideration. By the present amendment, non-elected claims 17-26 are canceled without prejudice. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the present amendments, claims 5-16 are pending and under consideration.

Election/Restriction

Applicants affirm the election of Group I, claims 5-16 directed to methods for detecting the presence of lung cancer cells, classified in class 435, subclass 91.2.

Double Patenting

Claims 5-16 stand provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1-9, 17-18, 20, 21 and 22 of copending Application No. 11/392,479.

Applicants note that, in the Response to the Restriction Requirement filed in copending Application No. 11/392,479, on November 9, 2007, Applicants elected Group II, claims 34-37 and 46-47. For convenience, Applicants submit herewith a copy of a preliminary amendment filed on December 14, 2007, canceling non-elected claims 1-9, 17-18, 20, 21 and 22 in the copending application. Accordingly, Applicants submit that the rejection has been obviated and may be properly withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 5-16 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Henderson *et al.* (20020172952) in view of Wang *et al.* (20020052329; Wang '329) and

Wang *et al.* (20020099012; Wang '012) and further in view of Edwards and Gibbs (PCR Methods and Applications, vol. 3, pages S65-S75, 1994). Specifically, the Action asserts that the Henderson *et al.* reference and the two Wang *et al.* references disclose methods for detecting the presence of lung cancer cells and further disclose the individual cancer-associated markers as recited in the present claims. The Action concedes that these references do not teach methods wherein two or more cancer-associated markers are detected in the same biological sample. However, the Action asserts that methods for detecting multiple targets in a biological sample were well known in the prior art, as evidenced by Edwards and Gibbs. As such, the Action asserts that the skilled artisan at the time of the claimed invention, would have been motivated to modify the methods taught in the Henderson *et al.* and the two Wang *et al.* references to encompass the multiplex PCR as taught by Edwards and Gibbs for the obvious benefits of simultaneously detecting multiple targets from a single biological sample in a single assay and for the additional advantages as taught by Edwards and Gibbs, such as flexibility of experimental design and reduction in expense and time.

Applicants respectfully traverse the ground for rejection and submit that the presently claimed methods are not obvious in view of the cited art. In particular, Applicants submit that the cited references taken for what they teach as a whole do not teach or suggest the presently claimed methods for detecting lung cancer using multiple markers. As admitted by the Action, Henderson *et al.*, Wang '329 and Wang '012 do not teach or even suggest that the individual markers they each disclose could be used in combination with any other marker, let alone the markers specifically recited in the instant methods, to better detect cancer. The present invention centers on the discovery that when two or more of these markers are used together, they provide expanded detection of lung cancer (see, *e.g.*, Table 3, pages 31 and 32 of the published PCT application WO2004/084804). There is no indication in any of these references that these cancer-associated markers complement one another and provide expanded cancer detection when used together. Thus, Applicants submit that the skilled artisan, at the time of filing of the present invention, would not have had the requisite reasonable expectation that the combination of the individual lung cancer markers disclosed by Henderson *et al.*, Wang '329 and

Wang '012 would have provided any benefit whatsoever over any of the markers used individually.

Furthermore, Applicants submit that the disclosure of Edwards and Gibbs does not remedy these deficiencies in that this reference is, in fact, limited to discussion of multiplex PCR in the setting of detecting gene mutations/deletions, polymorphic repetitive DNA, and microbe detection and fails to provide any teaching or suggestion whatsoever with regard to detection of cancer by the complementation of multiple markers. Thus, contrary to the Action's assertion, the skilled artisan would not have had a reasonable expectation of any benefits of simultaneously detecting multiple targets from a single biological sample in a single assay such as flexibility of experimental design and reduction in expense and time.

Moreover, the United States Supreme Court recently noted that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 383 U.S. 39, 53-54 (April 30, 2007, No. 04-1350). Applied to the instant application, Applicants submit that even assuming *arguendo* that there was motivation to combine the independent elements of (i) the cited Henderson *et al.* and Wang *et al.* references, and (ii) the multiplex PCR methods of Edwards and Gibbs, such a combination unquestionably falls short of rendering obvious the presently claimed method for detecting the presence of lung cancer cells by detecting multiple cancer-associated markers. Nothing in the prior art would have permitted the person having ordinary skill to reasonably predict that the combination of the individual recited cancer-associated markers would provide the advantages of the presently claimed method.

Additionally, "[t]he Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a *predictable* result." *KSR*, citing *U.S. v. Adams*, 383 U.S. 39, 50-51 (1966) (emphasis added). It is respectfully submitted that the subject matter of the instant claims simply could not have been predicted by the prior art, where neither Henderson *et al.*, Wang *et al.* ('329) or Wang *et al.* ('012), each alone or in combination with any other knowledge in the prior art including Edwards and Gibbs, provide the requisite

reasonable expectation of success to the person of ordinary skill. On this point, prior to the instant application, it could not be predicted, *e.g.*, whether the detection of the recited cancer-associated markers combined would provide additional benefit over detection of each individually. As articulated by the Supreme Court, the presently recited combination thus does "more than yield a predictable result", and is therefore nonobvious.

There is simply no indication in the prior art that the recited markers complement one another in their ability to detect lung cancer in a biological sample. The skilled artisan would have had no way of knowing that combining the recited markers would provide any advantage whatsoever. Contrary to the Action's assertion, without the teachings of the present application, choosing and combining individual cancer-associated markers as taught in the cited art could have resulted in no added advantage in detection of lung cancer and could, in fact, have resulted in an increase in expense and time. Without the teachings of the present application, the skilled artisan would have had no way to reasonably predict whether the combination of these cancer-associated markers would be advantageous.

Accordingly and in view of the foregoing, Applicants submit that the instant claim satisfies the requirements of 35 U.S.C. § 103. Reconsideration and withdrawal of the rejection are respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

/Julie A. Urvater/
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JAU:ms

Enclosure:
Copy of Preliminary Amendment filed in copending Application No. 11/392,479

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This Preliminary Amendment copy is intended as an attachment to an Amendment for U.S. Application No. 10/550,797 filed July 26, 2006, attorney docket no. 210121.609USPC.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Barbara K. Zehentner-Wilkinson et al.
Application No.	:	11/392,479
Filed	:	March 29, 2006
Confirmation No.	:	6011
For	:	METHODS, COMPOSITIONS AND KITS FOR THE DETECTION AND MONITORING OF LUNG CANCER

Examiner	:	Molly E. Baughman
Art Unit	:	1637
Docket No.	:	210121.609C1
Date	:	December 14, 2007

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Commissioner for Patents:

Please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-33. (Canceled)

34. (Original) A composition for detecting cancer cells in a biological sample comprising at least two of:

a) a first oligonucleotide specific for L762P;

b) a second oligonucleotide specific for L550S;

c) a third oligonucleotide specific for L587S; and

d) a fourth oligonucleotide specific for L984P.

35. (Original) The composition of claim 34, wherein the first oligonucleotide is specific for an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, the second oligonucleotide is specific for an L550S nucleic acid sequence set forth in SEQ ID NO:5, the third oligonucleotide is specific for an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO:27, and the fourth oligonucleotide is specific for an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or 39 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4 or 40.

36. (Original) A diagnostic kit for detecting cancer cells in a biological sample comprising at least two of:

a) a first oligonucleotide specific for L762P;

b) a second oligonucleotide specific for L550S;

c) a third oligonucleotide specific for L587S; and

d) a fourth oligonucleotide specific for L984P.

37. (Original) The kit of claim 36, wherein the first oligonucleotide is specific for an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, the second oligonucleotide is specific for an L550S nucleic acid sequence set forth in SEQ ID NO:5, the third oligonucleotide is specific for an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and the fourth oligonucleotide is specific for an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or 39 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4 or 40.

38.-45. (Canceled)

46. (Original) An array comprising at least two of:

a) a first oligonucleotide specific for L762P;

b) a second oligonucleotide specific for L550S;

c) a third oligonucleotide specific for L587S; and

d) a fourth oligonucleotide specific for L984P.

47. (Original) The array of claim 46, wherein the first oligonucleotide is specific for an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, the second oligonucleotide is specific for an L550S nucleic acid sequence set forth in SEQ ID NO:5, the third oligonucleotide is specific for an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and the fourth oligonucleotide is specific for an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or 39 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4 or 40.

48.-53. (Canceled)

REMARKS

Prior to examination on the merits, please enter the above amendment in which non-elected claims 1-33, 38-45 and 48-53 have been canceled. The present amendment is made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Favorable consideration of the subject application is respectfully requested.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

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